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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/870,762	06/06/97	DUFT B	226/104

022249
LYON & LYON LLP
SUITE 4700
633 WEST FIFTH STREET
LOS ANGELES CA 90071-2066

HM12/1113

EXAMINER	
DEVI,S	
ART UNIT	**PAPER NUMBER**
1645	21

DATE MAILED: 11/13/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/870,762	Duft et al.
Examiner	**Group Art Unit**
S. Devi, Ph.D.	1645

☒ Responsive to communication(s) filed on *07/24/2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Change of Art Unit Location

1) Effective 20 June 2000, the Art Unit location of the instant application in the US PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1645.

Appeal Brief

2) In view of the Appeal Brief filed on 07/24/00 (paper no. 20), PROSECUTION IS HEREBY REOPENED. New and/or modified grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(a) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(b) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Status of Claims

3) Claims 1-6 are pending in the instant application and are under examination.

Co-pending Application

4) The Office has become aware of Applicants' co-pending application, SN 09/445,517, filed after the final rejection was mailed out in the instant case. In view of this, a provisional double patenting rejection is made below in paragraph 10.

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant

Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

7) The rejection of claims 1-3 made in paragraph 7 of the Office Action mailed 09/16/98 (paper no. 8) as being anticipated by Rink *et al.* (US 5,739,106) is withdrawn. Applicants are asked to note the modified rejection made below.

8) The rejection of claims 4-6 made in paragraph 9 of the Office Action mailed 09/16/98 (paper no. 8) as being unpatentable over Rink *et al.* ('106) in view of Gaeta *et al.* (US 5,686,411) is withdrawn.

9) The rejection of claims 1-6 made in paragraph 10 of the Office Action mailed 09/16/98 (paper no. 8) under 35 U.S.C. § 103(a) as being unpatentable over Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996) (I) or Kolterman *et al.* (WO 96/40220) (II) or Moyses *et al.* (*Diabetic Med.* 13: 34-38, September, 1996) or Thompson *et al.* (*Diabetes* 46: 632-636, April 1997) in view of Cooper *et al.* (*Biochim. Biophys. Acta* 1014(3): 247-258, 1989, abstract) and Rink *et al.* is withdrawn. Kolterman *et al.* (WO 96/40220) ('220) (II) has been used in a modified rejection made below.

Double Patenting Rejection(s)

10) The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal

disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

Instant claims are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of the co-pending application, SN 09/445,517. Although the conflicting claims are not identical, they are not patentably distinct from each other, because of the overlapping scope of the claims.

Rejection(s) under 35 U.S.C. § 103

11) Claims 1-3 are rejected under 35 U.S.C § 103(a) as being unpatentable over Rink *et al.* (US 5,739,106, already of record) ('106).

It is noted that the claimed method uses a composition comprising an anti-obesity agent consisting of either amylin **or** an amylin agonist. It is also noted that claims 1-3 do not recite any doses of amylin or amylin agonist. Claims 1-3 do not recite any routes of administration either.

Rink *et al.* ('106) illustrate that administration of amylin **alone** did suppress food intake in mice (see Figure 1). Figure 1 depicts that amylin alone when injected at 2 microgram/kg induced more than 50% inhibition in food intake at 30 minutes. Under 'Brief Description of the Drawings' in column 14, Rink *et al.* explicitly teach that rat amylin "alone" suppressed food intake.

Rink *et al.* ('106) differ from the instant invention in not using their method for treating "obesity" in a human subject.

However, a method of suppressing food intake in a subject using a compound can reasonably be viewed by one skilled in the art as a method of treating obesity, since a skilled artisan would understand that suppression of food intake would lead to loss of body weight. Further, given that the murine model is generally accepted in the art as predictive of reduction in weight gain or obesity, or suppression of food intake in humans, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use or extend Rink's ('106) method of suppressing food intake to another mammalian subject, such as a human subject, to produce the method of the instant invention, with a reasonable expectation of success. Since human clinical trials are often conducted following successful animal experimentation, a skilled artisan would have been motivated to produce the instant invention by extending Rink's ('106) method to humans for the expected benefit of suppressing food intake and thereby reducing weight gain or obesity in humans, as treating obesity in humans is generally highly

desired in the art.

A specific secondary reference teaching that animal models are generally accepted in the art as predictive of reduction in weight gain or obesity, or suppression of food intake in humans, is **not** applied in this rejection, since such a teaching is widely known to those skilled in the art. See the section 'Prior Art' below for animal models widely accepted in the art.

Claims 1-3 are *prima facie* obvious over the prior art of record.

12) Claims 1-4 are rejected under 35 U.S.C § 103(a) as being unpatentable over Arnelo *et al.* (Arnelo *et al. Am. J. Physiol.* 271: 6 pt 2: R1654-R1659, December 1996) (Arnelo *et al.* I), or Arnelo *et al.* (*Scand. J. Gastroenterol.* 31: 83-89, January 1996) (Arnelo *et al.* II).

It is noted that the claimed method uses a composition comprising an anti-obesity agent consisting of either amylin **or** an amylin agonist. It is also noted that claims 1-4 do not recite any doses of amylin or amylin agonist. Claims 1-3 do not recite any routes of administration either. In this rejection, the method of treatment of obesity is viewed as the same as the reduction in body weight in light of the experimental results presented in Example 1 of the instant specification.

Arnelo *et al.* (I) teach a method of reducing food intake or decreasing body weight gain, i.e., treating obesity, in rats by subcutaneous administration of a composition consisting of IAPP (i.e., amylin) in a vehicle (i.e., pharmaceutically acceptable carrier) containing saline (see abstract; page R1655 and page R1654, left column, last paragraph). The composition contains 7 or 25 or 50 pmol/kg/min (i.e., an effective amount) of IAPP, which significantly decreased body weight gain (see page R1656, right column; Figure 4, and page R1657, right column).

Arnelo *et al.* (II) teach a method of reducing body weight, i.e., treating obesity, by subcutaneous administration of 50 pmol/kg/min (i.e., an effective amount) of a composition consisting of IAPP (i.e., amylin) and a DMSO-containing saline to rats (see page 85, left column; page 84, both columns and abstract). The prior art method significantly decreased the body weight and food intake in amylin-treated rats (see page 86 and Figure 4). Arnelo *et al.* (II) further teach IAPP to be a satiety factor (see page 87, left column).

Arnelo *et al.* (I) or Arnelo *et al.* (II) differ from the instant invention in not using their method for decreasing weight gain or reducing food intake in a human subject.

However, given that the rat model is widely accepted in the art as predictive of weight

reduction in humans, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use or extend Arnelo's (I or II) method of decreasing body weight gain to another mammalian subject, such as a human subject, to produce the method of the instant invention, with a reasonable expectation of success. Since human clinical trials are often conducted following successful animal experimentation, a skilled artisan would have been motivated to produce the instant invention by extending Arnelo's method (I or II) to humans for the expected benefit of reducing the incidence of obesity in humans, as treating obesity in humans is highly desired in the art.

A specific secondary reference teaching that animal models are generally accepted in the art as predictive of reduction in weight gain or obesity, or suppression of food intake in humans, is **not** applied in this rejection, since such a teaching is widely known to those skilled in the art. See the section 'Prior Art' below for animal models widely accepted in the art.

Claims 1-4 are *prima facie* obvious over the prior art of record, absent evidence to the contrary.

13) Claims 5 and 6 are rejected under 35 U.S.C § 103(a) as being unpatentable over Arnelo *et al.* (Arnelo *et al. Am. J. Physiol.* 271: 6 pt 2: R1654-R1659, December 1996) (Arnelo *et al.* I), or Arnelo *et al.* (*Scand. J. Gastroenterol.* 31: 83-89, January 1996) (Arnelo *et al.* II) as applied to claims 4 and 1 above, and further in view of Bennett *et al.* (US 5,955,443).

The teachings of Arnelo *et al.* (I) or Arnelo *et al.* (II) modified as explained above do not disclose the use of 30-300 microgram/dose of amylin 1 to 4 times a day.

However, effective doses of a pharmaceutical compound and optimal frequency of its administration to a human subject can be readily determined by routine experimentation by those skilled in the art based on the age, sex, weight, clinical condition and extent of a clinical condition in a human subject, or can be determined by a medical practitioner on a case by case basis. Nothing more than a routine skill is needed for such a determination. For example, Bennett *et al.* teach that (see column 27, lines 32-45):

> Human doses can be extrapolated from animal studies (Katocs et al., Chapter 27 In: Remington's Pharmaceutical Sciences, 18th Ed., Gennaro, ed., Mack Publishing Co., Easton, Pa., 1990). Generally, the dosage required to provide an effective amount of a pharmaceutical composition, which can be adjusted by one skilled in the art, will vary depending on the age, health, physical condition, weight, type and extent of the

disease or disorder of the recipient, frequency of treatment, the nature of concurrent therapy (if any) and the nature and scope of the desired effect(s) (Nies et al., Chapter 3 In: Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Ed., Harman et al., eds., McGraw-Hill, New York, N.Y., 1996).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to arrive at the dose and the frequencies of administration of amylin in humans, as recited in claims 5 and 6, by routine experimentation or optimization, for use in Arnelo's (I) or Arnelo's (II) method as modified.

Claims 5 and 6 are *prima facie* obvious over the prior art of record.

14) Claims 1-6 are rejected under 35 U.S.C § 103 (a) as being unpatentable over Kolterman *et al.* (WO 96/40220, already of record) (Kolterman *et al.* II) in view of Meglasson (US 5,134,164).

It is noted that Example 1 of the instant specification enables the claimed method for reducing weight in patients having type II diabetes mellitus.

Kolterman *et al.* (II) teach a method of treating type II diabetes mellitus comprising administering a therapeutically effective amount of an amylin agonist, such as, ^{25,28,29}pro-h-amylin, s-calcitonin and h-amylin. Administration is preferably by subcutaneous injection (abstract and claims). Amylin agonists, such as, ^{25,28,29}pro-h-amylin, may be administered in single or multiple doses, for example, two (BID), three (TID), and/or four (QID) times per day. BID doses range from about 30 μg to 150 μg BID, more preferably from about 50 μg to 60 μg BID. TID doses range from about 30 μg to 150 μg, more preferably about 60 μg TID. QID doses range from about 30 μg to 60 μg QID, more preferably about 30 μg QID. These doses have been demonstrated to be effective in various human clinical trials and are administered subcutaneously (see page 21). Kolterman *et al.* teach that type II diabetes mellitus is characterized by hyperglycemia (see page 7, lines 12 and 13) and that AC137 (i.e., ^{25,28,29}pro-h-amylin) induces reduction in hyperglycemia in type II diabetic patients (see claims 2, 7 and 11, and pages 12-14).

Kolterman *et al.* (II) do not expressly state that their method is also useful in the treatment of obesity.

However, that Kolterman *et al*'s (II) method also serves as a method of treatment of obesity is implicit from the teachings of Kolterman *et al.* (II) in light of what is well known in the art. For instance, Meglasson discloses that hyperglycemia occurs in obesity and non-insulin

dependent diabetes mellitus (NIDDM) (see column 1, third paragraph). It is taught that excess adiposity can be seen in NIDDM associated with obesity and obesity without NIDDM (see column 2, first sentence). Most importantly, Meglasson explicitly teaches that a compound that is useful in the treatment of hyperglycemia "could also be used to treat or prevent NIDDM" and "obesity" (see column 2, lines 21-25).

Given that amylin agonist, ^{25,28,29}pro-h-amylin, has already been identified in the art as a compound that is useful in the treatment of hyperglycemia and NIDDM, or as a compound that reduces hyperglycemia in patients with type II diabetes, i.e., NIDDM, as taught by Koltermann *et al.* (II), it would have been obvious to one of ordinary skill in the art at the time the invention was made to use Kolterman's (II) method of reducing hyperglycemia for treating obesity to produce the instant invention, with a reasonable expectation of success, because Meglasson explicitly teaches that any compound that is useful in the treatment of hyperglycemia could also be used to treat or prevent obesity. A skilled artisan would understand that Kolterman's anti-hyperglycemic compound, ^{25,28,29}pro-h-amylin (i.e., an amylin agonist analogue), would also serve as an anti-obesity agent. Since there is an art-recognized general need for reducing the incidence of human obesity in general and/or diabetic population, one skilled in the art would have been motivated to use Kolterman's method of reducing hyperglycemia in humans to treat obesity for the expected benefit of reducing the increasing incidence obesity, because Meglasson explicitly teaches that any compound that is useful in the treatment of hyperglycemia could also be used to treat or prevent obesity.

Claims 1-6 are *prima facie* obvious over the prior art of record.

Response to Applicants' Arguments

15) The arguments advanced by Applicants in their Appeal Brief filed 07/24/2000 are moot in light of the Office's withdrawal or modification of the previous art rejections. However, for the record, the Office is addressing herebelow some of Applicants statements and misstatements made in the Appeal Brief.

(A) Applicants state that the Office does not mention of patents '014 (US 5,280,014) and '841 (US 5,364,841) in the rejection of the instant claims that are directed to the use of

amylin agonists in the treatment of obesity, an invention which is supported with human clinical data (see paragraph bridging pages 5 and 6). Applicants further allege that the Office used the '014 and '841 patents "introduced by the Applicants" to rebut the rejection to lodge a rejection.

For the record, US patents '014 and '841 were originally **undisclosed** to the Office by the Applicants. These patents were not "introduced by the Applicants" as Applicants misstate, but were first made of record as relevant prior art by the Office via the first action on the merits mailed 09/16/98 (see page 8). The two patents were applied in the rejection of claims 1 and 2 before claim 1 was amended by Applicants (see page 6 of the Office Action mailed 06/24/99), since the two patents teach a method of treatment of obesity in a subject comprising administering to a subject an effective amount of CGRP 8-37, which is also known to serve as an *amylin agonist* in addition to having amylin antagonistic activities.

Contrary to the Applicants' statement, there is no clinical data in the instant specification showing amylin as an anti-obesity agent.

(B) Applicants state that the doses of amylin agonist claimed in the instant application are taught by the applied art, US patent 5,739,106, to have no effect on appetite suppression. Applicants further indicate, on page 12 of their Appeal Brief, that Rink *et al.* do not teach the subcutaneous injection of amylin.

For the record, US patent 5,739,106 was applied under 35 U.S.C 102(e) to reject claims 1-3, which do not recite any route of administration of amylin or amylin agonist or the doses to be administered. The term "subcutaneous" does not even appear in claims 1-3. Furthermore, claims 1-3 are not limited to the use of amylin agonist in a method of treatment of obesity, but these claims also encompass the use of an alternative compound, amylin, in the treatment of obesity. US patent 5,739,106 explicitly discloses that amylin alone inhibits food intake (see paragraph 9 above). Applicants ignore the results demonstrated in Figure 1 of Rink *et al.*, which show >50% inhibition in food intake when a certain dose of amylin alone was administered to rats (see closed circles in Figure 1).

With regard to the Applicants' statement on the lack of teaching of subcutaneous administration by Rink *et al.*, ('106), Applicants' attention is drawn to column 20, first paragraph under 'Formulations', where Rink *et al.* teach that their formulation may be provided in a form

suitable for subcutaneous administration.

(C) Applicants further state that the composition in the Rink patent includes amylin agonist "admixed" with a CCK agonist (see page 12 of the Appeal Brief) and that Rink is directed to appetite suppression in rodents using combinational formulations and "not amylin alone" (page 29 of the Appeal Brief).

Contrary to the Applicants' statement, Rink *et al.* teach that an amylin agonist may be more advantageously administered **separately** from a.CCK agonist (see column 20, first paragraph under 'Formulations'), thus indicating that amylin agonist is administered alone. Furthermore, Figure 1 of Rink *et al.* shows >50% inhibition in food intake when a certain dose of amylin alone was administered to rats (see closed circles).

(D) On pages 13 and 14 of the Appeal Brief, Applicants discuss about the claimed 30-300 micrograms per dose of amylin or amylin agonist and the doses used by Rink *et al.*, and conclude that Rink *et al.* do not anticipate the claims within the meaning of 35 U.S.C. § 102.

However, instant claims 1-3, which were rejected previously under 35 U.S.C. § 102(e), do not recite any doses of amylin or amylin agonist. Claims 1-3 do not recite any routes of administration either.

(E) Applicants state that obesity and diabetes "have only an occasional coincidence" (see page 21 of Applicants' Appeal Brief).

However, the art indicates just the opposite. For instance, the following prior art references teach that NIDDM is frequently closely associated with obesity :

- Griver *et al.* (*Nutrition Res.* 14: 465-483, 1994) teach that the non-insulin-dependent (NIDDM) form of diabetes is "often" associated with obesity (see abstract).
- Stogdale (*Cornell Vet.* 76: 156-174, 1986) teaches that obesity is "frequently" associated with NIDDM (see abstract).
- Scheen (*Drugs* 54: 355-368, September 1997) teaches that obesity is a condition "frequently" associated with NIDDM (see abstract).
- Johnston *et al.* (*J. Hypertension* 10: 393-397, 1992) teach that obesity and NIDDM are "often associated" (see abstract).
- Thomas *et al.* (*Circulation* 91: 764-770, 1995) teach the association between

NIDDM and obesity (see abstract).

- Lutz *et al.* (*Br. Vet. J.*149: 527-536, 1993) teach that obesity is a "frequent concomitant problem" in human Type 2 diabetes (see abstract).

- Meglasson (US 5,134,164) teach that excess adiposity is an etiological factor in NIDDM and when extreme represents a disease state in itself (see abstract).

It is important to note in this regard that the only example in the instant application that enables the claimed method of treating obesity using the amylin agonist, pramlintide, is in patients having type II diabetes mellitus or NIDDM (see Example 1).

(F) At the end of page 17, Applicants state that, effective May 29, 2000 for applications filed after November 29, 2000, the new statutory changes to 35 U.S.C. § 103(c) under the American Inventors Protection Act of 1999 have the effect of disqualifying commonly owned or obligated art as of the date of invention. Therefore, Applicants contend that the Office statement regarding Rink *et al.* and Gaeta *et al.* which were applied in a 35 U.S.C. § 103(a) rejection because they qualify under 35 U.S.C. § 102(e), no longer holds true.

Applicants are correct in that new statutory changes would be applicable to those applications filed **after** November 29, 2000. However, the instant application was filed in **1997** and hence Rink *et al.* and Gaeta *et al.* have been properly applied in a 35 U.S.C. § 103(a) to reject the instant claims.

(G) On page 24 of the Appeal Brief, Applicants contend that diabetes treatment and obesity treatment do not belong to the same art. Applicants' attention is directed to the reference of Meglasson (US 5,134,164) and the modified rejection made above using Meglasson's reference and Kolterman's (II) reference, which clearly shows that diabetes treatment and obesity treatment both belong to the analogous art. See also the prior art references cited in paragraph 13(E), which show that diabetes and obesity are frequently clinically closely associated.

(H) Applicants have mischaracterized the teachings of Cooper *et al.* as applied by the Office to reject instant claims under 35 U.S.C. § 103(a). In one of the 35 U.S.C. 103(a) rejections of record, Cooper *et al.* was **not** applied because it taught the use of amylin antagonists to treat obesity. Instant claims are **not** directed to a method of treating obesity using an amylin

antagonist. Instead, Cooper *et al.* was cited as a secondary reference in a 35 U.S.C. § 103(a) solely to document that it is known in the art that obesity frequently accompanies type 2 diabetes mellitus (NIDDM) and that the art recognizes obesity to be a result of NIDDM (see page 6 of the Office Action mailed 09/16/98). The 5th full paragraph on page 6 of the Office Action mailed 09/16/98 explains Cooper's teachings and it did not even mention the word "antagonist".

Applicants further allege that the Office maintains the instant rejection based on the Cooper reference (see page 31 of the Appeal Brief, last paragraph). However, the rejection was not based on Cooper's reference alone. Cooper *et al.* was cited as one of the secondary references along with several other references to make a point unrelated to amylin antagonists.

(I) On page 3 of the Appeal Brief, Applicants state that Amylin Pharmaceuticals' scientists are the authors of all the publications relied on by the Office in formulating the rejections and that all of the information used by the Office in considering the rejection of claims in the instant application is based upon inventions made at Amylin Pharmaceuticals, Inc.

It should be noted in this regard that the rejections of record were properly made since the applied references qualified as prior art under the cited statutes, based on their date of publication or disclosure, and the different inventive entity status. Some of the new rejections made in this Office Action appear to show that scientists other than those from Amylin Pharmaceuticals Inc. have taught the subcutaneous use of amylin in reducing body weight and food intake.

Prior Art

16) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Kleyn *et al.* (US 6,043,346) disclose that obesity poses a major worldwide health problem (see column 4, lines 22 and 23). Kleyn *et al.* teach that animal-based body weight disorder systems, i.e., tub mice models, may be used to identify compounds capable of ameliorating body weight disorder-like symptoms. Such animal models may be used as test substrates for the identification of drugs, pharmaceuticals, therapies and interventions which may be effective in treating such disorders. For example, animal models may be exposed to a compound, suspected of exhibiting an ability to ameliorate body weight disorder symptoms, at a sufficient concentration and for a time sufficient to elicit such an amelioration of body weight

disorder symptoms in the exposed animals. The response of the animals to the exposure may be monitored by assessing the reversal of disorders associated with body weight disorders such as obesity. With regard to intervention, any treatments which reverse any aspect of body weight disorder-like symptoms should be considered as candidates for human body weight disorder therapeutic intervention. Dosages of test agents may be determined by deriving dose-response curves (see column 32, fourth full paragraph).

- Venkatesan (US 6,020,361) teaches compounds which show much higher antiobesity and antihyperglycemic activity in animal models and conclude that such compounds are useful in treating diabetes, hyperglycemia, and obesity in humans and animals, when formulated into pharmaceutical compositions (see column 2, lines 10-24).

- Korsgaard *et al.* (US 6,008,242) teach a rabbit model of obesity and state that it is a generally recognized model of obesity. The data obtained with an anti-obesity agent in a rabbit model are taught to be useful in using the agent as a therapeutic agent against obesity in mammals, including primates such as humans (see column 2).

- Tartaglia *et al.* (US 5,972,621) teach that animal-based body weight disorder systems, which may include, for example, ob, db and ob/db mice, may be used to identify compounds capable of ameliorating body weight disorder-like symptoms. Such animal models may be used as test substrates for the identification of drugs, pharmaceuticals, therapies and interventions which may be effective in treating such disorders. For example, animal models may be exposed to a compound, suspected of exhibiting an ability to ameliorate body weight disorder symptoms, at a sufficient concentration and for a time sufficient to elicit such an amelioration of body weight disorder symptoms in the exposed animals. The response of the animals to the exposure may be monitored by assessing the reversal of disorders associated with body weight disorders such as obesity. With regard to intervention, any treatments which reverse any aspect of body weight disorder-like symptoms should be considered as candidates for human body weight disorder therapeutic intervention. Dosages of test agents may be determined by deriving dose-response curves (see column 38).

- Lee *et al.* (US 5,932,779) teach a method of identifying compounds for ameliorating body weight disorders by testing in animal model systems for body weight. Lee *et*

al. teach that animal models may be used as test substrates for the identification of drugs, pharmaceuticals, therapies and interventions which may be effective in treating such disorders. Lee *et al.* teach that animal models may be exposed to a compound, suspected of exhibiting an ability to ameliorate body weight disorder symptoms, at a sufficient concentration and for a time sufficient to elicit such an amelioration of body weight: disorder symptoms in the exposed animals. The response of the animals to the exposure may be monitored by assessing the reversal of disorders associated with body weight disorders such as obesity. With regard to intervention, Lee *et al.* teach that any treatments which reverse any aspect of body weight disorder-like symptoms should be considered as candidates for human body weight disorder therapeutic intervention. Dosages of test agents may be determined by deriving dose-response curves (see abstract and column 16).

- Morley *et al.* (*Am. J. Physiol.* 267: R178-R184, July 1994 - already of record) teach that amylin is effective in reducing food intake in genetically obese (ob/ob) and lean (ob/c) mice and diabetic (db/db) and lean (db/c) mice. It is taught that amylin effectively suppresses food intake because it is a peripherally acting satiety agent (see abstract).

- Shuldiner *et al.* (US 5,877,283) disclose a method for treatment of obesity and type II diabetes mellitus. Shuldiner *et al.* identify obesity as a primary health concern amongst industrialized countries (see abstract and column 1, last paragraph).

- Taylor *et al.* (US 5,830,434) disclose preferred rat and mouse animal models of hyperglycemia and obesity which could be used for screening for the efficacy of various compounds to treat NIDDM (see column 7, first full paragraph). Taylor *et al.* further disclose how one of ordinary skill in the art can determine the dosage of these compounds (see column 6, lines 10-16):

> The exact dosage may vary on the basis of the patient's age, weight, size and general overall condition and a physician would best be able to determine the exact dosage according to these parameters. Further guidance on determining dosages and modes of administration are available as provided in Remington's Pharmaceutical Sciences (13).

- Svec *et al.* (US 5,527,788) teach obesity as a major health problem of the Western world having medical and economic importance (see column 1, lines 24-28). Svec *et al.* disclose a rat model of obesity which shares many characteristics with human obesity, including

hyperglycemia and insulin resistance (see column 7, lines 33-39).

- Wilkison *et al.* (US 6,100,047) disclose that obesity and diabetes animal models can be used to determine the relevance of selective molecules in treating human obesity (see column 4, first full paragraph).

- Cooper *et al.* (US 5,124,314 - already of record) disclose that DAPP or amylin "may be found to have clinical utility, such as, appetite suppressant activity (see column 1, lines 57-62).

Remarks

17) Claims 1-6 stand rejected. This is a non-final rejection.

18) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week.

19) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD
S. Devi
Patent Examiner
October 2000

L. F. Smith
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